

PATENT SPECIFICATION

(1) 1 372 040

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(54) TABLETS

(71) We, BOEHRINGER INGELHEIM G.m.b.H., a German Body Corporate of Ingelheim am Rhein, Germany, do hereby declare the invention for which we pray
 5 that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

The present invention relates to coated
 10 sustained release tablets.

Numerous pharmaceutical substances are quickly absorbed in the gastro-intestinal tract of humans and of animals and, subsequently, quickly eliminated. This means
 15 that the action of such pharmaceutical substances is in general only of short duration.

In order to ensure that the activity of a pharmaceutical substance extends over a long period and to avoid the necessity of repeatedly taking tablets within short time intervals, tablets with sustained release have been developed. These are characterised by releasing the pharmaceutical substance only slowly while passing through
 25 the patient's gastro-intestinal tract. It would be ideal if for the production of such sustained release forms the differing degrees of absorption in the several sections of the gastro-intestinal tract could be taken into
 30 consideration. As the degree of absorption taking place within a particular section of the gastro-intestinal tract depends among other things upon the speed of passage of the pharmaceutical substance through the tract and the surface as well as numerous permeability criteria, it is understandable
 35 that not all these factors can be observed. For this as well as technological reasons concerning the large scale production of such sustained release forms, the production has been restricted to sustained release forms which simply release the active ingredient gradually over a long period of time.

45 In this connection, sustained release

forms have for example been known containing the active ingredient within a structure containing an insoluble substance. The active ingredient can thus be covered on both sides with a layer of the insoluble substance (see for example Austrian Patent No. 205,671). As indicated in the Austrian Patent and confirmed by trials, constant release of the active ingredient per unit time is not achieved. The sustained release shows rather an exponential decrease with time. This is readily understood when one bears in mind that the tablet surface coming into contact with its environment becomes continuously smaller.

Another form of table, developed with the aim of obtaining a homogeneous release of substance per unit time over a period of several hours, has been described in U.S. Patent No. 3,146,169 and in the corresponding German Patent No. 1,298,238. In this case a tablet core comprising the active ingredient is covered with an insoluble and indigestible coat by means of pressure coating, and a circular hole is formed at one place in the tablet. As described therein, and proved by *in vitro* trials, a release of active ingredient takes place through this hole such that in equal periods of time equal quantities of substance dissolve and are therefore available for absorption. This means, that the cumulative release of active ingredient increases linearly with time. This form of sustained release, however, is only useful for active ingredients absorbed to an equal extent in each of the various intestinal sections.

There are numerous substances the absorption of which clearly decreases during their passage through the gastro-intestinal tract, and which, starting from the stomach, are absorbed less and less in the small intestine, the farther through they go.

In order to obtain a constant pharma-